



Mitral annulus calcification and sudden death

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ABSTRACT

Mitral valve annulus calcification is a degenerative cardiac condition often found at autopsy in the elderly. While usually considered incidental to the cause of death, we report two cases where mitral valve annulus calcification with valve stenosis was associated with sudden death. Case 1: a 61-year-old female who had underlying atherosclerosis and hypertension collapsed at home. At autopsy there was marked mitral valve annulus calcification with valve stenosis and cardiomegaly. Case 2: a previously well 74-year-old female collapsed in a toilet. At autopsy there was marked calcification of the mitral valve annulus with valve stenosis. In both cases death was attributed to the effects of the calcified mitral valve annulus. Although such calcification may be unrelated to the terminal lethal mechanism, the association with left atrial enlargement, atrial fibrillation, mitral regurgitation, mitral stenosis, bacterial endocarditis, ischaemic and thromboembolic stroke, myocardial infarction, and arrhythmias, means that it should not be overlooked in the differential diagnosis in cases of sudden and unexpected death.

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1. Introduction

Mitral valve annulus calcification (MAC) is a degenerative condition commonly seen in older individuals, especially women. Autopsy series report an overall incidence of 8.5%¹ in those aged over 50. While macroscopically evident disease is uncommon in those under 70 years of age^{2,3} it is increasingly common with advancing age with an incidence of 43.5% in women over 90 years.¹ Although the finding of mitral valve annulus calcification is often considered an incidental finding clinically and at autopsy, we report two cases in which this condition was associated with unexpected death.

2. Case reports

Case 1: a 61-year-old woman who had experienced recent mobility difficulties reported feeling short of breath requiring a nebuliser, and then collapsed in bed 10 min later. She had a past history of type 2 diabetes mellitus, hypercholesterolaemia, hypertension and a possible previous myocardial infarction.

At autopsy the major findings included marked calcification of the mitral valve annulus (Fig. 1), with mitral valve stenosis and atrial dilatation, cardiomegaly (500 g) with left ventricular hypertrophy,

bilateral pleural effusions and pulmonary oedema. There was narrowing of the right coronary artery ostium and calcific but not stenotic coronary artery atherosclerosis. The abdominal aorta showed marked calcific atherosclerosis with stenosis of the left renal artery. Histology showed focal interstitial fibrosis of the myocardium but there was no evidence of acute ischaemic damage. Death was attributed to mitral valve annulus calcification with valve stenosis in association with cardiac hypertrophy and atherosclerosis.

Case 2: a 74-year-old, previously-well, woman collapsed in the toilet. There was no significant past medical history. At autopsy, the major finding was marked calcification of the mitral ring annulus, involving particularly the posterior leaflet with associated mitral valve stenosis and left atrial dilatation. Other cardiovascular findings included a dysplastic anterior mitral valve leaflet, moderate atherosclerosis with approximately 50% stenosis of the left anterior descending coronary artery and calcific abdominal aortic atherosclerosis. There was no gross or histological evidence of acute or chronic myocardial ischaemic changes and the heart was not significantly enlarged (406 g). No other underlying organic disease was present that had contributed to the death. Death was attributed to mitral valve annulus calcification with valve stenosis.

3. Discussion

MAC is a common autopsy finding in the elderly and is often considered an incidental finding of little practical importance.^{1,3,4} However, while mild disease is usually of no clinical significance, increasing severity may be associated with potentially lethal

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Fig. 1. Marked calcification of the mitral valve annulus with prominent exophytic calcific deposits causing protrusion of a leaflet.

complications.^{5–7} Specifically, MAC may be associated with left atrial enlargement, atrial fibrillation, mitral regurgitation, mitral stenosis, bacterial endocarditis, ischaemic and thromboembolic stroke, myocardial infarction, arrhythmias and sudden death.^{1,4–15}

Calcification of the mitral annulus is often clinically silent but may present with a systolic cardiac murmur, or be incidentally detected on chest radiograph when the classic 'J', 'C' or 'U' shaped density is noted in the posterior aspect of the cardiac shadow.^{8,10,12} MAC may also be diagnosed premortem on echocardiogram.^{10,12}

Calcification of the mitral valve annulus commences with deposition of calcium aggregates in the angle between the ventricular endocardium and the valve leaflet insertion, with eventual coalescence and formation of a bar of calcification, typically behind the posterior valve leaflet.^{1–3} At autopsy one may see a small nodule or localised spicule of calcification in mild cases, or a rigid bar of calcification measuring up to 2 cm in diameter which may involve the entire valve annulus in those with more severe disease.^{1–3} The posterior aspect of the annulus is more frequently involved and advanced cases often show displacement of the posterior mitral leaflet into the left atrium.^{1,4} Microscopy reveals amorphous basophilic deposits surrounded by fibrous tissue and often an inflammatory reaction.^{1–3} Rare cases have shown metaplastic cartilage formation and occasional cases may have central caseation.^{1–3}

Cardiac conduction defects have been reported in association with mitral annular calcification since Bonninger first described the entity in association with complete heart block in 1908.^{1,4,8,10} Cardiac conduction defects include atrioventricular block, intra-ventricular conduction defects, bundle branch blocks and complete heart block.^{1,5,6,8–10,12} The high rate of conduction defects most likely relates to the close spatial relationship between the deposited calcified material on the posterior aspect of the annulus and the adjacent atrioventricular node and bundle of His. These deposits can extend deep into the adjacent left atrial myocardium to disrupt the interatrial conduction system, the left ventricle to disrupt the atrioventricular conduction system or into the membranous aspect of the intraventricular septum to disrupt the bundle of His and its main branches.¹²

Severe calcification may cause valve dysfunction in the form of both mitral stenosis and incompetence.^{4,8,14,15} Mitral regurgitation results from annular calcification causing ring rigidity with subsequent interference with ring contractility.^{1,4,8,14,15} Less commonly MAC can lead to mitral stenosis,^{5,8,10,15} as was observed in the two reported cases. In such cases there is marked calcification of the annulus with either fixation of the valve leaflets or a reduction in

the size of the valve orifice due to the calcific mass protruding into the ventricular chamber.^{8,15}

While it could be assumed that the association of MAC with mitral valve dysfunction would result in a high incidence of cardiac failure¹² other factors may be involved. For example, in a study of 370 hearts obtained from routine hospital autopsies Pomerance found a higher incidence of MAC in patients with cardiac failure compared to those without⁴ but most of these cases showed additional cardiac disease, with only 3% of those in cardiac failure having MAC as the sole pathology. He concluded that MAC was likely to be only one of a number of factors in the pathogenesis of congestive cardiac failure. In the reported cases, case 1 displayed cardiomegaly with features of congestive cardiac failure including pleural effusions and pulmonary congestion. The decedent also had a history of hypertension and possible prior myocardial infarction. However, in case 2 MAC was the major lesion.

Endocarditis and thromboembolic events may occur in association with MAC^{1,6,16} as calcific nodules can ulcerate and provide a site for thrombi to form, with the potential for resultant thromboembolic stroke. They may also act as the nidus for development of infective endocarditis.¹⁵

While the above mechanisms are clear, other associations between MAC and cardiovascular death are less well understood. For example, the Framingham Heart Study and the Northern Manhattan Study showed a statistically significant increase in all causes of cardiovascular death, including myocardial infarction and coronary insufficiency, in those with MAC. When adjusted for other risk factors for cardiovascular disease^{7,11} a 1.6 increase for overall cardiovascular death remained which correlated with increasing severity of disease.⁷

Although it has been postulated that MAC is associated with an increased incidence of cerebrovascular accidents, the Northern Manhattan Study and the Framingham Heart Study found the association between MAC and ischaemic stroke to be either unfounded or of borderline significance.^{7,11} However, the Cardiovascular Health Study did find a statistically significant increased incidence of ischaemic stroke in elderly patients with MAC compared to those without.¹³

Thus many authors note the importance of MAC as a measure of cardiovascular disease risk,^{7,9} with some authors even suggesting that MAC is a form of atherosclerosis, citing the similar histological features in arterial atherosclerosis and MAC.⁹ Despite this association and the shared risk factors, severe MAC can occur independently to severe coronary artery atherosclerosis as was seen in case 2.

In summary, MAC is a relatively common degenerative condition in the elderly. While it may be an incidental finding at autopsy, MAC, especially when severe, can lead to cardiovascular complications which may significantly contribute to, or be primarily responsible for, sudden death.

Conflict of interest

None declared.

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Ethical approval

None.

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